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**Osteopontin deficiency does not prevent but promotes alcoholic neutrophilic hepatitis in mice.**

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**Public Summary:**

We developed mouse models to test preventive effect of novel target in alcohol-associated liver diseases.

**Scientific Abstract:**

Alcoholic hepatitis (AH) is a distinct spectrum of alcoholic liver disease (ALD) with intense neutrophilic (polymorphonuclear; PMN) inflammation and high mortality. Although a recent study implicates osteopontin (SPP1) in AH, SPP1 is also shown to have protective effects on experimental ALD. To address this unsettled question, we examined the effects of SPP1 deficiency in male mice given 40% calories derived from ad libitum consumption of the Western diet high in cholesterol and saturated fat and the rest from intragastric feeding of alcohol diet without or with weekly alcohol binge. Weekly binge in this new hybrid feeding model shifts chronic ASH with macrophage inflammation and perisinusoidal and pericellular fibrosis to AH in 57% (15 of 26) of mice, accompanied by inductions of chemokines (Spp1, Cxcl1, and interleukin [IL]-17a), progenitor genes (Cd133, Cd24, Nanog, and epithelial cell adhesion molecule), PMN infiltration, and clinical features of AH, such as hypoalbuminemia, bilirubinemia, and splenomegaly. SPP1 deficiency does not reduce AH incidence and inductions of progenitor and fibrogenic genes, but rather enhances the IL-17a induction and PMN infiltration in some mice. Furthermore, in the absence of SPP1, chronic ASH mice without weekly binge begin to develop AH. CONCLUSION: These results suggest that SPP1 has a protective, rather than causal, role for experimental AH reproduced in our model.

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